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Pyrexia in cats: retrospective analysis of signalment, clinical investigations,
diagnosis and influence of prior treatment in 106 referred cases

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Key words: fever, feline, infectious peritonitis, inflammatory, immune mediated, neoplastic

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Abstract

Objectives To describe the features and diagnoses of a population of cats referred with pyrexia. Other aims were to report, and evaluate the utility of, clinical investigations performed, and describe any effect of treatment before referral on temperature at presentation and ability to make a diagnosis.

Methods Clinical records of cats with pyrexia ($\geq 39.2^{\circ}\text{C}$) documented at least twice were retrospectively reviewed. Cases were assigned into disease categories (infectious, inflammatory, immune-mediated, neoplastic, miscellaneous and no diagnosis [pyrexia of unknown origin, PUO]) based on diagnosis. The overall value of clinical investigations was assessed by classifying them as ‘enabling’, ‘assisting’ or ‘no assistance’ in achieving each diagnosis. The effect of treatment before referral was assessed for any association with temperature at presentation and ability to make a diagnosis (PUO versus other disease categories).

Results 106 cases were identified. The most common cause of pyrexia was feline infectious peritonitis (22 cats, 20.8%) and the largest disease category was infectious (41/106, 38.7%). Inflammatory conditions were found in 19 (17.9%), neoplasia in 13 (12.3%), miscellaneous causes in 11 (10.4%) and immune-mediated disease in six (5.7%) cats. No diagnosis was reached in 16 (15.0%) cats, often despite extensive diagnostic investigations. Cytology and histopathology most often ‘enabled’ or ‘assisted’ in obtaining a diagnosis. Most cats (91 cats, 85.8%) received treatment before referral, with antimicrobial treatment given to eighty-

49 seven (82.1%) cats. Prior treatment before referral was not associated with temperature at
50 presentation nor with success in establishing a diagnosis.

51

52 **Conclusions and relevance** This is the first study investigating causes of pyrexia in cats.

53 Infectious diseases were most common and immune-mediated diseases were comparatively
54 rare.

55

56

57 Introduction

58 Pyrexia (fever) is an increased body temperature secondary to the release of
59 pyrogens and a raised thermoregulatory set point in the anterior hypothalamus¹. It is part
60 of the non-specific adaptive response of the body to disease and is thought to confer a
61 significant evolutionary advantage. However, there are disadvantages of pyrexia and these
62 tend to outweigh benefits when pyrexia becomes more severe or prolonged¹. Pyrexia that
63 remains undiagnosed despite investigations is referred to as pyrexia of unknown origin
64 (PUO). Over 200 diseases have been associated with PUO in humans². Precise definitions of
65 PUO vary; extrapolating from human medicine, PUO in dogs and cats has been defined as
66 a temperature of $\geq 39.2^{\circ}\text{C}$ (102.5°F) of at least three weeks duration in which no obvious
67 cause is found following at least three visits to the veterinary surgeon and/or three days of
68 hospitalisation (including basic evaluation of history, clinical signs, physical examination
69 and diagnostic testing [complete blood count, serum biochemistry, urinalysis])¹.
70 Recommendations regarding the diagnostic approach to pyrexia have been described in
71 cats^{1, 3, 4}, but as no studies investigating causes of pyrexia have been published in cats, such
72 recommendations are experience-based rather than evidence-based. It has been stated that
73 infectious causes are the most common reason for feline pyrexia^{3, 5} but no published
74 evidence exists. Immune-mediated disease is known to be the most common cause of
75 pyrexia in dogs⁶⁻⁸.

76 The aims of the present study were to describe the population characteristics of cats
77 with pyrexia referred to two veterinary referral centres and to identify the causes of pyrexia.
78 Further objectives were to report the clinical investigations performed and evaluate their

- 79 usefulness in obtaining a diagnosis, and to describe treatments given before referral and
- 80 their possible effect on temperature at presentation and ability to reach a diagnosis.

81 Methods

82 The clinical databases of feline patients referred to the Small Animal Hospital,
83 University of Bristol and the Small Animal Hospital, University of Glasgow January 2011-
84 June 2015 were retrospectively searched to identify cats with pyrexia. Databases and
85 clinician case logs were searched using the terms 'pyrexia', 'pyrexia', 'PUO' and 'fever'. Case
86 records were then retrospectively reviewed (SS) and appropriate details entered into a
87 spreadsheet (Excel for Windows, Microsoft). Details regarding signalment, history, physical
88 examination and minimum database were obtained in all cats. Peak temperature
89 documented by the referring veterinarian within the past month and temperature at
90 presentation to the referral centre were recorded. Further diagnostic investigations were
91 performed depending on clinical presentation and the attending clinician's discretion. To
92 be included pyrexia (rectal temperature $\geq 39.2^{\circ}\text{C}$ [102.56°F]) had to have been documented
93 at least twice (to reduce the risk of cats with stress hyperthermia being included), including
94 at least once at the referring veterinary practice. Cases were excluded if records were
95 inadequate.

96 The study was approved by the University of Bristol's Animal Welfare and Ethical
97 Review Body (veterinary investigation number [VIN] 16/019) and the University of
98 Glasgow's Research Ethics Committee (37a/16).

99

100 *Treatment before referral*

101 Any drug administered by the referring practice after the initial documentation of
102 pyrexia was recorded. As this included a large range of drugs, individual agents were
103 grouped into therapeutic classes: non-steroidal anti-inflammatory drugs (NSAIDs),

104 antimicrobials, corticosteroids, opioid analgesics, 'supportive' gastrointestinal medications
105 (e.g, antiemetics, antacids), and miscellaneous drugs.

106

107 *Diagnostic investigations*

108 Investigations performed by the referring veterinarian and at the referral centre were
109 recorded. For the purpose of analysis, neutrophilia was graded as mild (12 to $<20 \times 10^9/l$),
110 moderate (20 to $<30 \times 10^9/l$) or severe ($\geq 30 \times 10^9/l$); neutropenia was defined as $<4 \times 10^9/L$.
111 Anaemia was classified as mild (PCV 20 to $\leq 24\%$), moderate (15 to $<20\%$), or severe ($<15\%$).
112 Increases in alanine aminotransferase (ALT) were graded as mild (<2 times upper reference
113 range), moderate (≥ 2 to 3 times), or severe (>3 times). Hypoalbuminaemia was classified as
114 mild (20 to <24 g/l), moderate (16 to <20 g/l), or severe (<16 g/l).

115 Imaging techniques included ultrasonography, radiography, CT, MRI and
116 endoscopy. Cytological examination was performed on fine needle aspirates from any
117 abnormal masses or enlarged lymph nodes. Feline immunodeficiency virus (FIV) antibody
118 and feline leukaemia virus (FeLV) antigen testing was initially performed using Petchek
119 ELISA (IDEXX) or FeLV/FIV SNAP (IDEXX), with polymerase chain reaction (PCR) testing
120 and/or virus isolation performed if results were positive.

121 Each diagnostic investigation was retrospectively categorised as: 'enabled' a
122 diagnosis, 'assisted' a diagnosis, or of 'no assistance'⁷. In cases where a negative result
123 contributed to a diagnosis, the test was reported as 'assisted' a diagnosis. A complete blood
124 count and serum biochemistry were performed in all cats, their usefulness in obtaining a
125 diagnosis was not examined.

126

127 *Cause of pyrexia: disease groups*

128 Cats were retrospectively assigned into one of the following disease groups based on
129 final diagnosis: infectious, inflammatory, immune-mediated, neoplasia, miscellaneous and
130 no diagnosis reached (PUO). Where more than one disease process from different categories
131 was diagnosed, the disease attributed to be the cause of the pyrexia was classified. When
132 this was unclear, cases were defined as miscellaneous.

133

134 *Outcome*

135 Whether cats survived to discharge, were euthanased or died was recorded.

136

137 *Statistical analysis*

138 Statistical analysis was performed using SPSS for Windows v23 (IBM Corp).
139 Descriptive statistics were prepared for all evaluated variables. Kolmogorov-Smirnov tests
140 were used to test for normality; continuous variables were reported as means and standard
141 deviations (sd) if normally distributed, and as medians and ranges if not normally
142 distributed.

143 Overall treatment before referral (yes/no) was assessed for association with
144 temperature at presentation using a T-test. Treatment was assessed for association with
145 success in making a diagnosis (i.e, PUO [no diagnosis] vs all other disease categories
146 [diagnosis reached]) using χ^2 test. Significance was defined as $P < 0.05$.

147

148 Results

149 One hundred and six cats met the inclusion criteria.

150

151 *Signalment*

152 Of the 106 cats, the most common breed was domestic (69 [65.1%]; 64 [60.4%]
153 domestic shorthair, five [4.7%] domestic longhair); the remaining 37 (34.9%) cats were
154 pedigrees. These comprised seven (6.6%) Ragdolls, six (5.7%) Bengals, six (5.7%) British
155 shorthairs, five (4.7%) Birmans, four (3.8%) Maine coons, three (2.8%) Siamese, and one each
156 (0.9%) of Balinese, Devon Rex, Korat, Oriental, Persian and Russian Blue. Median age was
157 4.0 years (10 weeks–15 years).

158

159 *History and treatment before referral*

160 Diagnosis was known or suspected at the time of referral in 11 (10.3%) cats; these
161 tended to be infectious (e.g. pyothorax, pyelonephritis, cellulitis), lymphoma (2 cats), or
162 structural disease (e.g. ureteral obstruction, intestinal intussusception). Regarding cats with
163 feline infectious peritonitis (FIP), two of 22 referring veterinarians mentioned FIP as a
164 possible diagnosis at referral. Ninety-one cats (87.5%) received treatment before referral;
165 treatment data were unavailable for two cases. Treatment had been given within 24-hours
166 of referral in 77 (74.0%) cats. Antimicrobials were administered in 87 cats (83.7%) (Table 1);
167 of these, 54 received one antimicrobial, 28 received antimicrobials from two different
168 classes, and five from three different classes. Almost two-thirds of cats received NSAIDs
169 (67/104, 64.4%) and approximately one-quarter received corticosteroids (25/104, 24.0%).
170 Opioid analgesia was administered to 30 cats (28.8%), 26 cats (25.0%) received

171 gastrointestinal support medication, and 20 cats (19.2%) received other miscellaneous
172 drugs.

173 Mean (\pm sd) peak temperature documented before referral was 40.1°C (\pm 0.5°C).
174 Pyrexia was reported to be present for a median of four days (1-168 days) before
175 presentation. Eighty one cats (76.4%) were pyrexia at referral and mean temperature at
176 presentation was 39.7°C (\pm 0.6°C). Overall treatment before referral was not associated with
177 temperature at presentation ($P=0.543$), nor with success in reaching a diagnosis ($P=0.999$).
178 As pyrexia associated with FIP is expected to be refractory to treatment, the association of
179 treatment before referral was also assessed in non-FIP cats only, and no significant
180 association was found (unpublished data).

181

182 *Diagnostic investigations*

183 The number of cats in which diagnostic investigations were performed and the
184 usefulness of investigations in obtaining a diagnosis are shown in Table 2. Complete blood
185 count and serum biochemistry were performed in all cats (results were unavailable in two
186 cases). The most common abnormalities were neutrophil abnormalities and anaemia on
187 complete blood count, and increased ALT and hypoalbuminaemia (Table 3) on serum
188 biochemistry.

189

190 *Disease categories*

191 Final diagnoses and disease categories are listed in Table 4. Infectious disease
192 represented the largest category (41/106, 38.7%). Within this category, FIP was diagnosed in

193 22 cases. Inflammatory (non-infectious) disease comprised the second most common
194 disease category (19/106, 17.9%) and neoplastic disease third (13/106, 12.3%). Pyrexia was
195 attributable to miscellaneous conditions in 11 cats (10.4%). Immune-mediated disease was
196 the smallest disease category (6/106, 5.7%). No diagnosis (PUO) was established in 16 cases
197 (15.1%). The median ages of cats in each disease category are described in Table 5.

198

199 *Outcome*

200 Cats were hospitalised for a mean of 5.0 days (± 3.2 days). Over two-thirds of cats
201 (71/106, 67.0%) survived to discharge, 31 (29.2%) cats were euthanased and four (3.8%) died
202 during hospitalisation.

203

204 Discussion

205 This is this first published survey describing causes of pyrexia in referred cats. To the
206 authors' knowledge, there are no similar surveys of pyrexia in first opinion practice.
207 Our study will therefore provide a useful comparison for future, ideally prospective, studies
208 of pyrexia in both the first opinion, and referral, setting. Using the same grouping
209 system previously described in a canine study⁷, we found infection to be the most common
210 disease category. In contrast, immune-mediated disease was most commonly diagnosed in
211 referral populations of pyrexia dogs^{6, 7}. Infection is the most common cause for pyrexia in
212 people².

213 In terms of specific conditions, FIP was the most common diagnosis. Diagnosis was
214 based on compatible clinicopathological findings and histopathology or positive feline
215 coronavirus immunostaining^{9,10}. Intermittent fever is one of the earliest signs of FIP⁹ and in
216 one study body temperature exceeded 39.5°C in 81% of cats with FIP, and over 40°C in
217 almost half of cases¹⁰. FIP remains a difficult disease to definitively diagnose, perhaps in
218 part due to the fluctuating nature of pyrexia meaning fever and clinical signs may falsely
219 appear to respond to antimicrobials, delaying investigation and/or diagnosis. The high
220 prevalence of FIP in this population where so many cats had received antimicrobials
221 (\pm NSAIDs) highlights the condition as the most common cause of pyrexia refractory to
222 empirical treatment. It is important to note that the prevalence of FIP may be abnormally
223 high as the participating institutions actively participate in FIP research, possibly resulting
224 in a biased population; it has been suggested that differences in disease category prevalence
225 in canine studies has been in part due to particular interests of the authors^{6, 11}.

226 Apart from FIP, few other specific infections were diagnosed in this study, despite
227 FIV/FeLV testing, *Toxoplasma gondii* serology and other infectious disease PCR tests being
228 commonly performed. This likely reflects the low prevalence of specific infectious diseases
229 in the UK, especially at referral level, although it may also reflect inappropriate test selection
230 by the clinician. The poor overall diagnostic value of routine serological and immunological
231 tests is well known in human medicine and there is debate over the minimal serological
232 tests indicated in PUO patients, due to the low prevalence of implicated diseases².

233 Inflammatory (non-infectious) conditions comprised the second most common
234 disease category in pyrexia cats, and interestingly, were almost as common as infectious
235 causes when FIP cases were not considered. The widespread use of antimicrobials in this
236 population may have resulted in infectious causes being incorrectly classified as
237 inflammatory (e.g. sterile versus non-sterile cellulitis, bacterial versus non-bacterial
238 cholelithiasis). This is a limitation inherent in the retrospective nature of the study and
239 may have resulted in an underestimation of infectious disease prevalence.

240 Neoplasia as a cause for pyrexia was seen in 12.3% cats, comparable to figures
241 described in pyrexia dogs (9.5%⁶ and 7.6%⁷). Unsurprisingly, as the most common feline
242 neoplasm, lymphoma was the most prevalent neoplasm in this study. Primary pulmonary
243 tumours were the second most frequent, found in three cats, and have previously been
244 reported to cause pyrexia¹¹, likely because of their propensity to become necrotic due to
245 their often large and solid nature.

246 Immune-mediated disease appears to be a less common cause for pyrexia in cats than
247 in dogs⁶⁻⁸, with only immune-mediated haemolytic anaemia and immune-mediated
248 polyarthritis diagnosed in our population.

249 Despite often extensive investigations, a definitive diagnosis was not reached in 15%
250 of cases., comparable to canine studies^{6, 7}. We hypothesise that cats with PUO had self-
251 limiting infections or transient inflammatory foci. In the present study, although most cats
252 were referred without a known diagnosis (and often referred to as having PUO by the
253 referring veterinarian), a cause was found in 85% of cases. The term 'PUO' should therefore
254 be reserved for cases where extensive diagnostics have failed to identify the cause. Not all
255 cases of PUO in this study met the definition proposed by Ramsey & Tasker (2017)¹, as only
256 four out of 16 cats had a duration of illness of more than three weeks. This is perhaps not
257 surprising as investigations and treatment are likely to be instigated much earlier than three
258 weeks in order to reduce patient morbidity.

259 Due to the retrospective nature of the study and assessment of survival data to
260 discharge only, it was not possible to assess if PUO was associated with outcome. Overall
261 survival to discharge (67.0%) was comparable however to a high (70%) survival rate
262 reported in dogs with miscellaneous causes for pyrexia⁶. The majority of humans with PUO
263 will eventually spontaneously recover¹².

264 No association between treatment and success in reaching a diagnosis was found.
265 Treatment before referral was not associated with temperature at presentation, in contrast
266 to dogs where prior treatment reduced the prevalence of pyrexia at the time of referral⁷.
267 This study also reported that the treatment of pyrexia was associated with a longer time to

268 diagnosis⁷. Because of this, and the proposed protective benefit of pyrexia, it has been
269 recommended to reserve antipyretic drugs for cases where body temperature exceeds 41°C
270 or clinical signs attributable to fever are severe¹.

271 Broad-spectrum antimicrobials are widely recommended for all cases of unexplained
272 pyrexia in dogs and cats^{1,3,11}, and in keeping with this recommendation, antimicrobials were
273 the most commonly administered drugs given before referral in this study, in over 80% of
274 cats. Furthermore, nearly one-third of all cats had received drugs from multiple
275 antimicrobial classes by the time of referral. The prevalence of bacterial infections as a cause
276 of pyrexia in first opinion veterinary practice may be sufficiently high to warrant such
277 treatment, although no evidence exists to support this. Withholding antimicrobials in stable
278 patients where fever is acute and mild is recommended in human medicine¹². Of note,
279 despite infections being regarded as (and shown to be in this study) the most common cause
280 of feline pyrexia, almost one-quarter of cats had received corticosteroids before referral.

281 A wide range of diagnostic investigations were employed to discern the cause of
282 pyrexia. Complete blood count and serum biochemistry were performed in all cases but the
283 most common abnormalities found (neutrophilia, increased ALT, anaemia and
284 hypoalbuminaemia) were non-specific. Abdominal ultrasonography was the most
285 commonly performed diagnostic procedure which 'enabled' or 'assisted' with a diagnosis
286 in over half of the cats in which it was employed. Thoracic imaging (radiography and/or
287 CT) was performed in over half of cats and appeared to be less useful than abdominal
288 ultrasonography. Echocardiography was performed in approximately one-third of cats but
289 only assisted with diagnosis in one cat (diagnosed with myocarditis); indeed it was

290 seemingly performed in the majority of cases to assess for concurrent cardiac disease due to
291 the detection of a heart murmur or gallop sounds, as well as to assess for endocarditis. Our
292 data suggests that diagnostic imaging selection in pyrexia cats should depend on localising
293 signs (eg, MRI of the brain 'assisted' or 'enabled' a diagnosis in all cases presented with
294 neurological signs) rather than seeking abnormalities without appropriate localisation.

295 Fluid (pleural or peritoneal) analysis was a highly useful diagnostic test when
296 performed, likely due to its importance in aiding FIP diagnosis. Cytology and
297 histopathology were widely employed and were very useful diagnostic procedures, in
298 agreement with canine studies⁶⁻⁸. Bacterial culture (eg, of fluid, tissue) 'enabled' or 'assisted'
299 with a diagnosis in approximately one-third of cases in which it was performed, although
300 false negative results may have occurred due to previous antimicrobial therapy or difficulty
301 in culturing certain organisms (e.g. *Mycoplasma* spp.). Interestingly, blood culture was
302 performed in only one cat and even though this test is often recommended when
303 investigating feline pyrexia^{3,11} it does not appear to be a principal test required for diagnosis.
304 Feline pancreatic lipase immunoreactivity was performed in over one-quarter of cats, likely
305 due to its widespread availability as a bench-side test and due to the non-specific clinical
306 signs of feline pancreatitis (anorexia, lethargy). Its usefulness in obtaining a diagnosis was
307 fairly low, however, perhaps due to pancreatitis being an uncommon cause of pyrexia,
308 and/or due to the test's limitations in diagnosing chronic or mild forms of the condition¹³.

309 The study's population comprised referral cases and therefore likely contained cases
310 where fever did not spontaneously resolve or respond to empirical treatment, where
311 localising signs were absent, where simple diagnostic tests failed to identify a cause, or

312 alternatively where a diagnosis was known but intensive management was required.
313 Ultimately many patients were found to have relatively common conditions (e.g,
314 pancreatitis, lymphoma, cellulitis) and merely had an unusual or early manifestation of
315 these diseases that hindered diagnosis prior to referral.

316 Limitations of this study are largely due to its retrospective nature. Future studies
317 should focus on a prospective cohort of cats being referred with pyrexia. A larger number
318 of cases would also enable statistical tests to be performed to further investigate features of
319 the different disease categories and the diagnostic investigations performed. Appropriate
320 cases may have been missed due to the search methods employed (e.g, misspelling of
321 pyrexia) and incomplete records meant that some cases had to be excluded. Interpretation
322 of records was required in some instances to determine the final diagnosis and disease
323 category classification. Follow-up data were limited in that only survival to discharge was
324 known in the majority of cases. Finally, despite the endeavour to exclude hyperthermic cats,
325 it is still possible that some cases (particularly cats with respiratory impairment) may have
326 been hyperthermic. Furthermore, a few conditions diagnosed in this study have not been
327 previously associated with pyrexia (e.g, renal pseudocysts, uroliths, gastrointestinal foreign
328 bodies); while it is feasible pyrexia may occur in these conditions due to inflammation
329 and/or associated infection, hyperthermia cannot be fully excluded. Rectal temperature in
330 healthy cats can reach 39.3°C in the veterinary consultation room due to stress¹⁴. The
331 inclusion criteria of two or more documented episodes of increased rectal temperature was
332 used in an attempt to exclude cases with stress hyperthermia.

333

334 Conclusions

335 This is the first descriptive study investigating cases of feline pyrexia. A diligent
336 search for an infectious cause, particularly FIP, remains a priority in the investigation of cats
337 with pyrexia. In contrast to dogs, immune-mediated disease is a rare cause for feline
338 pyrexia. Abdominal ultrasonography and cytology are likely to be useful and readily
339 available diagnostic procedures. The administration of more than one antimicrobial class
340 was common in this population.

341

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344

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347

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350 authorship, and/or publication of this article.

351

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354 of this article.

355 Table 1. Antimicrobials administered before referral in a population of 106 cats with
 356 pyrexia
 357

| | |
|---|----|
| One antimicrobial administered (n=54) | |
| AC | 35 |
| Cefovecin | 9 |
| Fluoroquinolone | 4 |
| Clindamycin | 4 |
| Two antimicrobials administered (n=28) | |
| AC / fluoroquinolone | 12 |
| AC / metronidazole | 6 |
| AC / cefovecin | 3 |
| AC / doxycycline | 3 |
| AC / clindamycin | 1 |
| Fluoroquinolone / cefovecin | 1 |
| Fluoroquinolone / TMPS | 1 |
| Fluoroquinolone / clindamycin | 1 |
| Three or more antimicrobials administered (n=5) | |
| AC / cefovecin / metronidazole | 2 |
| AC / cefovecin / clindamycin | 2 |
| AC / cefovecin / doxycycline / fluoroquinolone | 1 |

358
 359 AC = amoxicillin-clavulanic acid; TMPS = trimethoprim sulfonamide
 360 Numbers (n) indicate number of cats

| Test | Number of cats in which test was performed (percentage) | Number of cats in which test 'Enabled a diagnosis' (percentage) | Number of cats in which test 'Assisted a diagnosis' (percentage) |
|---|---|--|---|
| Urinalysis | 46 (43.4%) | 0 | 2 (4.3%) |
| Urine culture | 31 (29.2%) | 3 (9.7%) | 0 |
| FeLV/FIV testing | 74 (69.8%) | FIV positive = 3 (4.0%) | 0 |
| Feline PLI | 28 (26.4%) | 3 (10.7%) | 0 |
| Abdominal ultrasonography | 74 (69.8%) | 11 (14.9%) | 28 (37.8%) |
| Abdominal CT | 9 (8.5%) | 0 | 1 (11.1%) |
| Thoracic radiography | 39 (36.8%) | 0 | 7 (18.9%) |
| Thoracic CT | 26 (24.5%) | 1 (3.8%) | 6 (23.1%) |
| Echocardiography | 33 (31.1%) | 0 | 0 (concurrent cardiomyopathy = 3) |
| MRI | 7 (6.6%) | 1 (14.3%) | 6 (85.7%) |
| Other imaging (e.g, CT/radiography of head, joints) | 7 (6.6%) | 1 (14.3%) | 6 (85.7%) |
| Endoscopy | Bronchoscopy 6 (5.7%) GI endoscopy 3 (2.8%) Rhinoscopy 1 (0.9%) | 1 (16.7%) | 3 (30%) |
| Bacterial culture (non-urine e.g, fluid, tissue) | 31 (29.2%) | 5 (16.1%) | 5 (16.1%) |
| Cytology | 43 (40.6%) | 16 (25.4%) | 12 (27.9%) |
| Body cavity fluid analysis | 30 (28.3%) | 5 (16.6%) | 19 (63.3%) |
| Histopathology | 26 (24.5%) | 13 (50.0%) | 7 (26.9%) |
| Faecal tests (culture, parasitology) | 8 (7.5%) | 0 | 3 (37.5%) |

| Test | Number of cats in which test was performed (percentage) | Number of cats in which test 'Enabled a diagnosis' (percentage) | Number of cats in which test 'Assisted a diagnosis' (percentage) |
|---|--|--|---|
| PCR (blood, tissue, saliva) | FCoV 15 (14.2%) Haemoplasma 8 (7.5%) <i>Mycoplasma felis</i> 5 (4.7%) FCV 5 (4.7%) FHV 4 (3.8%) <i>Toxoplasma gondii</i> 4 (3.8%) <i>Bordetella bronchiseptica</i> 4 (3.8%) <i>Tritrochomonas foetus</i> 1 (0.9%) <i>Mycobacteria</i> species 1 (0.9%) | 6 (12.8%) | 13 (27.7%) |
| Serology | <i>T. gondii</i> 22 (20.8%) FCoV 19 (18.8%) | 2 (4.9%) | 17 (41.4%) |
| Other tests performed but not further described | Alpha-1 glycoprotein, serum troponins, serum electrophoresis, bile acids, thyroxine, coagulation testing, serum cobalamin/folate, serum ammonia, electrocardiogram, gamma interferon testing, Coombs' testing, Ziehl Neelsen staining | | |

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FeLV = Feline leukemia virus, FIV = Feline immunodeficiency virus, PLI = pancreatic lipase immunoreactivity, GI = gastrointestinal, FCoV = Feline coronavirus, FCV = Feline calicivirus, FHV = Feline herpesvirus PCR = polymerase chain reaction

368 Table 3. Most common complete blood count and serum biochemistry abnormalities
 369 detected in 104 cats with pyrexia
 370

| Laboratory parameter | Number of cases |
|---|-----------------|
| Neutrophil abnormalities | 50 |
| Mild neutrophilia | 13 |
| Moderate neutrophilia | 14 |
| Severe neutrophilia | 9 |
| Band neutrophilia (normal overall neutrophil count) | 7 |
| Neutropenia | 7 |
| Anaemia | 39 |
| Mild | 18 |
| Moderate | 17 |
| Severe | 4 |
| Increased alanine transaminase (ALT) | 48 |
| Mild | 37 |
| Moderate | 9 |
| Severe | 2 |
| Hypoalbuminaemia | 32 |
| Mild | 14 |
| Moderate | 14 |
| Severe | 4 |

371
 372
 373 Neutrophilia: mild (12 to $<20 \times 10^9/l$), moderate (20 to $<30 \times 10^9/l$), severe ($\geq 30 \times 10^9/l$).
 374 Neutropenia: $<4 \times 10^9/L$. Anaemia: mild (PCV 20 to $\leq 24\%$), moderate (15 to $<20\%$), severe
 375 ($<15\%$). ALT: mild (<2 times upper reference range), moderate (≥ 2 to 3 times), severe (>3
 376 times). Hypoalbuminaemia: mild (20 to <24 g/l), moderate (16 to <20 g/l), severe (<6 g/l).
 377

378

379 Table 4. Final diagnosis and disease category classification for 106 cats with pyrexia

| Disease group | Diagnosis | Number of cats |
|--------------------|---|----------------|
| Infectious | FIP | 22 |
| | Cellulitis/otitis (media) | 4 |
| | Pyothorax | 3 |
| | Pyelonephritis/UTI | 3 |
| | Lower airway inflammation with <i>M. felis</i> | 2 |
| | Neutrophilic cholangiohepatitis | 2 |
| | Campylobacter enteritis | 2 |
| | Bronchopneumonia | 1 |
| | Brain empyema | 1 |
| | Hepatic abscess | 1 |
| | TOTAL | 41 (38.7%) |
| Inflammatory | Pancreatitis | 5 |
| | Sterile peritonitis | 3 |
| | Sterile lymphadenitis/panniculitis/cellulitis | 3 |
| | Inflammatory lower airway disease | 3 |
| | Lymphocytic cholangiohepatitis | 2 |
| | Inflammatory CNS disease | 2 |
| | Myocarditis | 1 |
| | TOTAL | 19 (17.9%) |
| Neoplasia | Lymphoma | 6 |
| | Pulmonary carcinoma | 3 |
| | Leukaemia (not characterised) | 2 |
| | Pulmonary metastases, primary neoplasm not identified | 1 |
| | Gastrointestinal adenocarcinoma | 1 |
| | TOTAL | 13 (12.3%) |
| Immune-mediated | Immune-mediated haemolytic anaemia | 3 |
| | Immune-mediated polyarthritis | 3 |
| | TOTAL | 6 (5.7%) |
| Miscellaneous | Intestinal obstruction (foreign body) | 3 |
| | Bone marrow disorder (not characterised) | 2 |
| | Ureterolithiasis/urolithiasis | 2 |
| | Intussusception | 1 |
| | Peri-renal pseudocysts | 1 |
| | Trauma | 1 |
| | Hippocampal necrosis | 1 |
| | TOTAL | 11 (10.4%) |
| No diagnosis (PUO) | TOTAL | 16 (15.0%) |

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382 FIP = Feline infectious peritonitis, UTI = urinary tract infection, CNS = central nervous
383 system, PUO = pyrexia of unknown origin

Table 5. Median age of 106 cats with pyrexia, as classified by disease category

| Disease groups | All cats | Infectious | Inflammatory | Neoplasia | Miscellaneous | Immune-mediated | No diagnosis (PUO) |
|----------------------------|----------------|----------------|----------------|----------------|---------------|-----------------|--------------------|
| Median (range) age (years) | 4.0 (0.2 – 15) | 2.5 (0.1-15.0) | 5.0 (0.6-12.0) | 8.0 (1.0-14.0) | 3.0 (0.6-8.0) | 8.5 (1.0-13.0) | 3.0 (0.1-14.0) |

PUO = pyrexia of unknown origin

References

- 1.Ramsey IK and Tasker S. Fever. In: Ettinger S, Feldman EC and Cote E, (eds.). *Textbook of Veterinary Internal Medicine*. 8th ed.: Elsevier, 2017, p. 195-203.
- 2.Knockaert DC, Vanderschueren S and Blockmans D. **Fever of unknown origin in adults: 40 years on.** *J Intern Med*. 2003; 253: 263-75.
- 3.Flood J. **The Diagnostic Approach to Fever of Unknown Origin in Cats.** *Comp Cont Ed Vet*. 2009; 31: 26-31.
- 4.Nelson RW and Couto CG. Fever of undetermined origin. *Small Animal Internal Medicine*. Canada: Elsevier, 2014, p. 1279-82.
- 5.Lappin M. Pyrexia and Hyperthermia. In: Harvey AM and Tasker S, (eds.). *BSAVA Manual of Feline Practice A Foundation Manual*. Gloucester: British Small Animal Veterinary Association, 2013, p. 287-9.
- 6.Dunn KJ and Dunn JK. **Diagnostic investigations in 101 dogs with pyrexia of unknown origin.** *J Small Anim Pract*. 1998; 39: 574-80.
- 7.Battersby IA, Murphy KF, Tasker S and Papasouliotis K. **Retrospective study of fever in dogs: laboratory testing, diagnoses and influence of prior treatment.** *J Small Anim Pract*. 2006; 47: 370-6.
- 8.Chervier C, Chabanne L, Godde M, Rodriguez-Pineiro MI, Deputte BL and Cadore JL. **Causes, diagnostic signs, and the utility of investigations of fever in dogs: 50 cases.** *Can Vet J*. 2012; 53: 525-30.
- 9.Pedersen NC. **A review of feline infectious peritonitis virus infection: 1963-2008.** *J Feline Med Surg*. 2009; 11: 225-58.

- 10.Riemer F, Kuehner KA, Ritz S, Sauter-Louis C and Hartmann K. **Clinical and laboratory features of cats with feline infectious peritonitis - a retrospective study of 231 confirmed cases (2000-2010).** *J Feline Med Surg.* 2016; 18: 348-56.
- 11.Lunn KF. Fever. In: Greene CE, (ed.). *Infectious Diseases of the Dog and Cat.* 4th ed. USA: Elsevier, 2012, p. 1115-23.
- 12.Mourad O, Palda V and Detsky AS. **A comprehensive evidence-based approach to fever of unknown origin.** *Arch Intern Med.* 2003; 163: 545-51.
- 13.Forman MA, Marks SL, De Cock HE, et al. **Evaluation of serum feline pancreatic lipase immunoreactivity and helical computed tomography versus conventional testing for the diagnosis of feline pancreatitis.** *J Vet Intern Med.* 2004; 18: 807-15.
- 14.Quimby JM, Smith ML and Lunn KF. **Evaluation of the effects of hospital visit stress on physiologic parameters in the cat.** *J Feline Med Surg.* 2011; 13: 733-7.